ROUNDUP360

Oncology

Proximal fibular tumours are as rare as hen's teeth

Primary bone tumours of the proximal fibula are rare, so rare that researchers in **Rochester (USA)** have reported the largest series of such tumours in the scientific literature. They aimed to characterise the natural history and presentation of these rare lesions. The researchers identified 112 patients between 1910 and 2007 presenting to the Mayo clinic with histopathologically confirmed proximal fibular tumours. Patients were for the most part young adults with a mean age of 27.6, the gender distribution was equal and patients were followed up for an average of 5.7 years. The most common histological diagnosis was osteosarcoma with the majority (86%) presenting with pain; other common findings included the presence of a palpable mass (51%) and common peroneal nerve palsy (12%). Surgical management was undertaken in 103 (92%) cases with 12 (11%) developing local recurrence. The most common surgical procedure was amputation (45%), and half of all patients in the series subsequently developed a distant metastasis. In those patients who underwent limb salvage (most commonly resection and lateral collateral ligament reconstruction) knee instability was not seen.[1] Although this is a rare tumour it is heartening to see a large series reporting good results for patients, including both those requiring amputation and those undergoing limb salvage. The high recurrence rates probably represent the historical nature of this series, where a large number of patients will not have received any adjuvant or neo-adjuvant treatment. It is reassuring to see that although many patients required primary amputation (as the tumours extend out into so many tissue compartments) those who underwent limb salvage achieved a good result.

If you have a hammer... then everything looks like a nail

The sharp-eyed readership of *360* will no doubt have noticed that this is the second paper from researchers in **Seoul (South Korea)** concerning navigation, and if you were as cynical as some of the *360* staff, you might wonder if the disappointing results reported in this month's Knee Roundup might have prompted this evaluation of the utility of computer navigation in bone tumour surgery. In what is the first report of navigated bone tumour surgery, the research team evaluated the functional and oncological outcomes for 18 serial patients who underwent navigation-assisted tumour resections. The research team report the results at a minimum of three years of follow-up for ten pelvic resections and eight joint-preserving procedures performed on 11 men and seven women. Navigation was used in patients requiring complex resections with stage IIB tumours (including osteosarcoma, chondrosarcoma, Ewing's sarcoma, malignant fibrous histocytoma and adamantinomas). All cases required complex resection, and the use of the navigation system in conjunction with pre-operative 3D imaging resulted in clear resection margins in all cases. The authors report an impressive three-year survival of 88.9% in all cases and 80% in pelvic malignancy. There were no recurrences in the metaphyseal lesions and two in the pelvic malignancies. However, there was a relatively poor event-free survival in keeping with the nature of the primary lesions at 66.7% (95% CI 44.9 to 88.5).[2] The authors present a compelling argument for the use of navigation in complex tumour resections, ensuring in these few reported cases clear tumour margins and consequentially potentially better prognosis. It is impossible to be certain of superior outcomes based on this small heterogeneous case series, however, here at *360* we may be using our now-redundant knee navigation systems for our tumour resections.

Radiotherapy-induced chondrosarcoma

The link between osteosarcoma and radiotherapy is so well established that it has become a staple of medical examinations. Amazingly however, there has never been, until now, conclusive evidence confirming the link. The difficulty with making this connection is that radiotherapy-associated 'second primary' tumours occur many years after initial exposure at a time when chondrosarcomas are common, which explains the difficulty in reaching a definitive answer. Researchers in **Rockville (USA)** designed a large study based on two large registries of cancer survivors to answer the question: are other types of bone sarcomas also caused by radiotherapy? The research team used data collated in the Surveillance Epidemiology and End Results cancer surveillance registries to establish the rates of all histologic types of bone sarcoma and compare these with known incidence rates in the general population. The researchers included 1.28 million patients collated on both registries between 1972 and 2008 who were adults and had survived five years post primary tumour. The research team used a poisson multivariate regression analysis to estimate relative risks associated with radiotherapy for subtypes of osteosarcoma and chondrosarcoma. The overall risk within the study population was calculated as standardised incidence ratios (SIR) for comparison with the background population. The research team identified 159 second bone sarcomas in the study population and an increased risk was noted in both those who did (257% excess risk SIR 3.57) and did not (25% excess risk SIR 1.25) receive radiotherapy. This pattern was seen in each histologic subtype, with higher SIRs in all radiotherapy groups. In patients with a second osteosarcoma the relative risk was 5.08 and 1.54 for chondrosarcoma; both of these relative risks were much higher for second tumours occur-

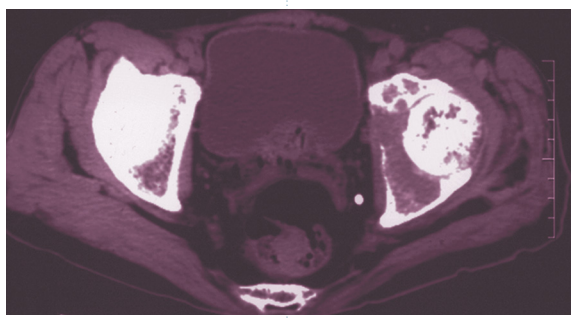
ring within the radiotherapy field.[3] In what must be one of the most impressive epidemiological studies in any area of medicine the research team must be congratulated for reporting over six million observed patient years and conclusively linking osteosarcoma to patients with a history of radiotherapy, in addition to establishing for the first time a smaller causal relationship to chondrosarcoma. This paper provides valuable information to inform post-radiotherapy surveillance programmes.

Mega-prostheses: solution or ticking time-bomb?

■ The management of large peri-articular bone tumours or metastasis is particularly challenging, often affecting young patients. Although arthroplasty offers the temptation of good clinical outcomes and high functional scores in otherwise difficult-to-salvage limbs, the long-term results of these mega-prostheses are poorly understood. The problem is particularly acute in knee mega-prostheses where the additional constraint required in linked or rotating hinge designs is known to lead to premature failure, even in older patients having surgery for degenerative joint diseases. Researchers from **Bologna (Italy)** have again stepped up to the plate and report the outcomes of 669 patients with musculoskeletal tumours of all types treated with tumour excision and reconstruction using a fixed hinge mega-prosthesis between 1983 and 2006. This prospective clinical cohort (Level III evidence) includes a mixture of 126 patients treated with the Kotz Modular Femur Tibia Reconstruction system (KMFTR) and HMRS (second generation) prosthesis. The HMRS is a revised design of the Kotz prosthesis which features an anatomical femoral stem with improved stress-shielding characteristics and a revised hinge design. Reconstruction was required in 474 distal femora, 163 proximal tibiae and 23 total femoral reconstructions. The authors report survival at ten and 20 years respectively, of 80% and 55%. Survivorship analysis with endpoints of breakage, aseptic loosening and polyethylene failure were 95% and 85%, 94% and 82% and 95% and 37%, respectively. The authors noted better survival to breakage of the HMRS prostheses, but no differences in other endpoints. Although this paper specifically concerns the survival of the implants, not the patients, the authors have previously reported disease-free survivorship in this cohort of 64% (424/669) and a significant rate of intra-operative complications including infection rates of up to 13%, and good or excellent results according to the Musculoskeletal Tumor Society outcome score of between 80% and 90% of patients.[4] It seems to us at *360* that the bar has been set with an excellently reported long-term follow-up of mega-prostheses for limb salvage surgery. However, this series does highlight the significant limitation of linked hinges: longevity. We await a similar long-term follow-up of the newer rotating hinge prosthesis which, by decoupling torsional forces, should reduce the failure rates and perhaps then provide a viable, functional, long-lasting option for patients who cannot have other forms of reconstruction. There is sadly a complete lack of well conducted randomised controlled trials assessing the major reconstructive options for peri-articular primary bone tumours. Until there is, we may never know which options to use for our patients.

CRP effectively predicts sarcoma survival

■ Perhaps the most difficult-to-answer question, both socially and medically, is the cancer patient asking, how long have I got? Prognosis, both in terms of disease-specific survival and local tumour control, is notoriously difficult, particularly in tricky tumours such as high-grade soft-tissue sarcomas. It was with no small measure of surprise that at *360* HQ we were passed this deceptively simple paper by the Editorial Board. Could CRP and co-morbidities really unlock the enigma of prognosis in sarcomas? A combined research team from **Birmingham (UK)** and **Tsu-city (Japan)** tackled this problem with a retrospective series of 332 patients with high-grade isolated sarcomas without metastatic spread. The prognostic value of the Charleson comorbidity index (CCI) and CRP levels measured prior to commencing therapy was established. The



research team established that raised CRP levels were seen in 46% (152/332) and CCI varied between 0 and 4. The authors identified that raised CRP was associated with a significantly poorer five-year disease-specific survival (42% raised *versus* 82% normal CRP). In addition, patients with raised CRP on admission had poorer local recurrence-free rates (75% *versus* 85%) and after correction for other potential confounders a multivariant analysis demonstrated CRP to be an independent predictor of survival. The investigators were unable to identify any association between the CCI and survival.[5] We are at a bit of a loss here at *360* to explain the clear association found by the research team between elevated CRP levels and disease-free survival. Nonetheless, this paper is an important step in untangling the difficulty of prognosis for patients suffering from high-grade sarcomas. Our hearty congratulations go to the research team.

Predicting survival in metastatic disease

■ Staying with the theme of survival prediction, a team from **Stockholm (Sweden)** and **Silver Spring (USA)** used data from the Scandinavian Skeletal Metastasis registry to attempt to externally validate the Bayesian-Estimated Tools for Survival (BETS) models. These were developed in the US to predict survival odds of patients with operable skeletal metastasis at three (BETS-3) and 12 months (BETS-12). The BETS models are based on prognostic variables (diagnosis, disease progression, patient factors and laboratory parameters). The model is complex and was developed using a machine-learned algorithm to produce two Bayesian classifiers with the aim of informing clinical decision making. The research team aimed to perform an external validation of the model using an independent dataset. The team used a ten-year cohort from the Scandinavian Metastasis Registry, including 815 patients with 12 months of survival data. The estimates of survival from the BETS models were assessed using the receiver-operating characteristic (ROC) analysis area under the curve (AUC). The BETS-3 model achieved an AUC of 0.79 and the BETS-12 model an AUC of 0.76. Analysis of incorrect predictions was undertaken and this was found to be more commonly optimistic than pessimistic.[6] The use of complex computer models can sometimes seem irrelevant in clinical practice, often difficult and time consuming to administer. Models that do

not provide reliable estimates of useful information often become little more than curios. However, these particular models have been deliberately developed to give accurate survival estimates to aid decision making in difficult clinical situations. When reaching a decision about prophylactic skeletal stabilisation, the patient's prognosis is crucial information to know. The validation of this model demonstrates it to be a good predictor of outcome at both three and 12 months. An AUC of > 0.75 is usually taken to represent a good prognostic score. We would encourage the authors to produce a simple 'App' to allow bedside and trauma conference calculation of BETS-3 and BETS-12 models.

MRI for recurrence in osteoid osteoma

■ The widespread success of radiofrequency ablation (RFA) of osteoid osteoma has improved the morbidity associated with surgery to treat the condition. However, it is not yet commonplace for patients to be managed primarily with RFA, which gives improved morbidity and is considered a successful intervention for this painful, difficult-to-treat lesion. Not content with just improving on treatment strategies, our radiology colleagues have now devised a clever little technique for assessing the success of RFA. A radiology team in **Aachen (Germany)** studied 20 consecutive patients undergoing RFA and undertook unenhanced and contrast-enhanced T1 weighted images of the lesion 24 hours after RFA had been performed. The research team used the signal-to-noise ratio (SNR) before and after they had administered the contrast.[7] In longer-term follow-up the authors identified that in 16 patients with SNR < 1.1 there was no local recurrence, while in four patients with a higher SNR, three recurrences were seen. It does appear that this form of contrast-enhanced MRI scan may give valuable information about the prediction of success in RFA. The authors venture the not unreasonable suggestion that in patients with a SNR increase of over 20%, immediate re-ablation may avert the majority of symptomatic tumour recurrences.

A sarcoma refresher

■ At *360* we would draw the attention of the readership to the latest European Sarcoma Network guidelines which provide a valuable refresher for the general orthopaedic surgeon.[8]

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